شبكة المعلومات الجامعية

بسم اللّه الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم باللّه العظيم أن المادة التي تم توثيقها وتسجيلها علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

ENVIRONMENTAL RISK FACTORS ON TELOMERE LENGTH MEASUREMENT OF ALZHELMER'S PATIENTS

Submitted By

Engy samir sayd soliman

B.Sc. of Science, (microbiology/Chemistry), Faculty of Science, Benha University, 2002

Master in Plants Science, (microbiology), Faculty of Science, Benha University, 2013

A Thesis Submitted in Partial Fulfillment
Of
The Requirement for the Doctor of Philosophy Degree
In
Environmental Sciences

Department of Environmental Basic Sciences
Institute of Environmental Studies and Research
Ain Shams University

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APPROVAL SHEET

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Engy Samir Sayed Soliman

Abstract

Background: Alzheimer's disease (AD) is genetic disorder disease. Regulation of Telomere Length (TL) is a result of complex interaction between environmental and genetic factors. **Aim:** Compare and evaluate between TL measurement by Florescence In Situ Hybridization (Q FISH) and Real Time- PCR .Study of some environmental risk factors in the development in AD. **Subjects and Methods:** This study included 30 AD patients and 10 controls. All blood samples were collected measured by using Q-FISH and RT-PCR to assess the telomere length. **Results:** Our data showed a significant difference in TL between AD patients and the controls P = 0.036. The correlation between results of Ratio of telomere repeat copy number to single copy gene copy number (T/S) ratio by RT-PCR and TL (Kb) by (Q-FISH) by linear regression analysis the correlation coefficient, r2 , for the relationship of T/S ratio to TL (KB) was =0.266 and P=0.004. **Conclusion:** A significant correlation was found between AD and telomere length shortening. Some environmental factors such as diabetes and hypertension influences on TL in AD. RT PCR is more accurate and easy than Q FISH.

Keywords: Alzheimer's disease, telomere length, Q-FISH, RT PCR, smoking, diabetes, hypertension, environmental influence.

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List of abbreviations

ΔCt	Delta Ct
r^2	correlation coefficient
AD	Alzheimer disease
APOE	Apo lipoprotein E gene
APP	Amyloid precursor protein
ATP	Adenosine triphosphate
BBB	Blood–brain barrier
Bp	Base pairs
CCD camera	Charged-coupled device
CT scan	Computed tomography scan
DAPI	4′,6-diamidino-2-phenylindole, is a Fluorescent Stain
DHA	A long-chain omega-3 fatty acid
DLB	Dementia with Lewy Bodies
DM	Diabetes mellitus
DNA	Deoxyribonucleic acid
FDA	Food and Drug Administration
Kb	Kilo base
MRI	Magnetic resonance imaging
PD	Parkinson's disease
PET scans	Positron emission tomography
PNA	Peptide nucleic acid
Q-FISH	Quantitative fluorescence in situ hybridization
RNA	Ribonucleic acid
RT -PCR	Real time polymerase chain reaction
SBP	Systolic blood pressure
STELA	Single telomere length analysis
T/C	Telomere/centromere chromosome 2
T/S	Ratio of telomere repeat copy number to single copy gene copy number
T2DM	Type-2 diabetes mellitus
TL	Telomere Length
TRF	Terminal Restriction Fragment
UCP	Uncoupling protein association
PBLs	peripheral blood leukocytes

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Introduction

The human brain is a remarkable organ that allows us to carry out every element of our daily lives. It manages many body functions, such as breathing, blood circulation, and digestion, without our prior knowledge or conscious direction. The brain embodies nerve cells and supportive glial cells, which hold the nerve cells in place and provide them with nutrients **(Forum et al., 2015).**

Alzheimer's disease (AD) is a neurological heterogeneous genetic disorder in which death of brain cells causes neurodegenerative symptoms such as memory loss and cognitive decline. The neurodegenerative symptoms of AD gradually worsen overtime with progressive shrinkage of the total brain size and decline of the number of nerve cells and their connections **(Barber, 2012).**

The brains of patients with AD have abnormal clumps of cellular debris, proteins (plaques) and collapsed microtubules, which normally support the structures inside the brain cells. Microtubule collapse is caused by a malfunctioning protein called tau. In Alzheimer's patients, tau proteins cluster together to form disabling plaques and tangles, which damage the healthy cells around them, leading to cell death **(John and Reddy, 2020).**

There are two main types of AD, the rare early-onset Alzheimer’s disease which usually affects people aged 30 to 60,some cases of early-onset disease are inherited and are called familial AD. The other type is late-onset Alzheimer’s disease, it is the more common form and occurs in those of 60 years and older. Gaining insight into the genetic factors associated with both forms of AD is important because

identifying genes that either cause the disease or influence a person's risk of developing it improves our ability to understand how and why the disease starts and progresses **(Bird, 2008) .**

There are several specific environmental risk factors in the development of AD as education, smoking, diabetes, obesity, hypertension, inflammation and Oxidative Stress **(Agnihotri and Aruoma, 2020).**

AD is a genetically heterogeneous disorder where AD2 (OMIM 104310), associated with the ApoE4 allele (107741) on chromosome 19; AD3 (OMIM 607822), caused by mutation in the presenilin-1 gene (PSEN1; OMIM 104311) on 14q and AD4 (OMIM 606889), is caused by a mutation in the PSEN2 gene (OMIM 600759) on 1q31 **(Corder et al.,1993).**

Telomeres are repeating DNA hexamer (TTAGGG) sequences found at the ends of chromosomes and are important for replication of the chromosomes during cell division. In each cell division telomeres are shortened, when become critically short chromosomes can undergo end fusions, aberrant recombination and degradation. Thus, maintenance of sufficient telomere length plays a major role in chromosomal stability and cell protection **(Muraki et al., 2012) .**

Short telomeres were associated with ageing and the development of age related diseases. Free radicals and oxidative stress for a long time can be involved in the ageing process. Telomere length is a marker for a person's ability to withstand DNA damage reflected by aging and oxidative stress **(Barth et al., 2020).**